REMARKS

Reconsideration of the present application in view of the above amendments and the following remarks is respectfully requested. Claims 1-17 are currently pending. Claims 8-17 have been withdrawn. Claims 1, 2, 3, and 7 have been amended for clarification purposes and to advance one aspect of the invention. New Claims 18-20 have been added. Support for the amendments can be found throughout the specification and at for example with respect to the new claims, claim 18 finds support at for example, page 33, lines 10-13 and claims 19 and 20 find support, at for example, page 35, lines 20-25. The above-amendments are made without prejudice to filing a continuation, continuation-in-part, or divisional thereon. No new matter has been added.

Election/Restriction

Applicants thank the Examiner for noting the species election. Accordingly, Applicants acknowledge that claims 1-17 are pending, claims 8-17 are drawn to a non-elected species and have been withdrawn, while claims 1-7 are currently being examined on the merits.

Objection to the Specification

The Examiner has objected to the specification as containing embedded hyperlinks in contravention of MPEP § 608.01. Applicants thank the Examiner for noting this informality. Accordingly, Applicants have amended the specification.

Brief Review of Certain Aspects of the Present Invention

The present invention relates *inter alia* to a method for determining the presence or absence of a disease or condition based on a visual pattern of markers captured concurrently by binding partners on a solid phase, rather than from single binding events. In the present case, the claims are particularly directed to a method for detecting a type of leukemia based on a visual

pattern of CD antigens captured by immunoglobulins specific for the CD antigens on a solid phase. The patterns of presence or absence of CD antigens are generated by the presence or absence of particular CD antigens in a sample from a patient and these CD antigens have been preselected to be discriminatory for a particular type of leukemia. It is the collective pattern of all binding events on a solid phase, *i.e.*, the pattern of presence or absence of these discriminatory CD antigen markers which is indicative of the type of leukemia (or absence of a type of leukemia) in a subject.

Applicants are seeking to protect a method of using an array assay device with immobilized immunoglobulin molecules directed to the discriminatory CD antigens which is indicative of a particular type of leukemia. The power of the methodology can be seen in the Venn diagrams attached as Exhibits 1 to 5 (Appendix I). To further illustrate this method, each sub-set of discriminatory CD antigens present on T-cells, B-cells, myeloid and stem cells are presented in Exhibits 2-5, respectively. In these Exhibits, a visual pattern based on the presence and absence of specific CD antigens is indicative of a specific leukemia divided from leukocytes of one of these subsets. In general terms, the pattern of captured discriminatory CD antigens using an array of immunoglobulins immobilized to a solid phase is visualized. These images may be analyzed by an iterative method which matches the pattern obtained from the sample to a library of standard patterns. Each standard or reference pattern is indicative of a type of leukemia and can be represented by different specific sub-sets of discriminatory CD antigens.

Rejections under 35 U.S.C. § 102(b)

Claims 1-7 stand rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by either Robbins *et al.*, Blood 82(4):1277-1287, 1993 or Valet *et al.*, Cytometry 20:275-288, 1997. In particular, the Action alleges that Robbins *et al.* teach a method of contacting samples with pairs of antibodies that are specific for CD antigens and further alleges that Robbins *et al.* teach a method of distinguishing HCL from CLL using CD19 and CD25 antibodies. Further, the Action asserts that Valet *et al.* teach detecting CD10, CD19, and CD23 and thus anticipates the presently claimed invention.

Applicants respectfully traverse these grounds for rejection. It is respectfully submitted that Robbins *et al.* describe the use of a two-color direct immunofluorescence assay to identify an immunophenotypic profile which allows sensitive and specific identification of hairy cell leukemia (HCL). In column 2 on page 1284, Robbins *et al.* conclude that two-color flow cytometry "is a useful adjunctive method" which will enhance the accuracy of diagnosis of HCL when used "in combination with routine morphology and TRAP staining". That paragraph goes on to discuss the use of a complete antibody panel to identify a single antibody marker.

The determination of a pattern of recognition from an extensive array of immunophenotypic CD antigens and the relative numbers of markers is a different concept to detecting the presence or absence of CD antigens by flow cytometry. We respectfully direct the Examiner to a peer reviewed clinical paper by the inventors published in *Cancer Research 60:* 4483-4489, 2001 (attached herewith as Appendix II) which describes the presently claimed concept in a clinical context. Although Robbins *et al.* use a two-antibody assay method which is distinctive of certain leukemia cells, they do not describe a panel of discriminatory antibodies which would permit pattern recognition. Consequently, Applicants consider that present Claim 1, is distinguishable over Robbins *et al.* since the claim requires that by determining which CD antigens bind to particular immobilized immunoglobulins, this establishes a pattern of presence or absence or level of particular CD antigens and this pattern is characteristic of a type of leukemia. Accordingly it is submitted that Robbins *et al.* do not disclose a pattern recognition assay for detecting leukemias.

Valet *et al.* describe a similar assay to that described by Robbins *et al.* although it describes a classification using a three-color immunocytometric technique. Again, as with the Robbins *et al.* article, it is respectfully submitted that at most Valet and Hoffkes disclose the essence of pattern recognition. It is more directed to the identification of particular cells based on certain uniquely expressed CD antigens as opposed to determining a pattern of interaction which is matched with a library of standard patterns, each characteristic of a particular leukemia as indicated in the Venn diagrams.

Accordingly, based on the comments above, Applicants respectfully submit that the present claims are novel over the cited art and thus request withdrawal of these grounds for rejection.

Claims 1-3 and 7 stand rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Terstappen (U.S. Patent No. 5,234,816). In particular, the Action alleges that Terstappen discloses a method for classifying leukemias comprising contacting samples with antibodies that bind to CD antigens.

Applicants respectfully traverse. It is respectfully submitted that Terstappen describe an immunophenotypic method based on monoclonal antibodies to certain CD antigens such as CD10, CD19, CD20, CD22, CD21, CD24, CD26, CD35, CD37, CD39, CD40, CD72, CD75, CD76 and CD79. Some of these CD antigens are recited in present Claim 3. A t column 3 of the subject patent, the invention is further described by dividing a biological sample into five aliquots and then using pairs of antibodies such as to CD10/CD19, CD20/CD5, CD3/CD22, CD7/CD3 and HLA-DR/CD13. This highlights the fundamental difference between this two-dimensional method as opposed to the multi-dimensional assay instantly claimed. Claim 1 of the present application contains the step of "determining which CD antigens have bound to which immoblized immunoglobulins to thereby establish a pattern of presence or absence or level of particular CD antigens, which pattern is characteristic of a type of leukaemia". Accordingly it is implicit within that step that a sufficient number of CD antigens is required to be assayed in order to determine the pattern of interaction.

As Terstappen does not teach the multi-dimensional assay presently claimed, Applicants submit that Terstappen does not include each an every limitation of the present claim and thus should not be a relevant novelty reference. Accordingly, Applicants respectfully request that the Examiner withdraw this ground of rejection.

Claims 1-3 and 7 stand rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Moreau *et al.*, Am. J. Clin. Pahol. 108:378-382, 1997, Matutes *et al.*, Blood 83(6):1558-1562, 1994, or Kurec *et al.*, British J. Haematology 81:45-51, 1992. More

specifically, the Action alleges that Moreau teaches a method for diagnosing CLL based upon a binding pattern to a panel of antibodies; Matutes allegedly teaches a method to distinguish splenic lymphoma from villous lymphocytes from CLL or HCL that includes antibody binding; and Kurec allegedly teaches immunophenotypic classification of CLL.

Applicants respectfully traverse these rejections and submit that again, for the reasons outlined above in relation to the other art documents, none of these three documents discloses a method based on pattern recognition and, hence, Applicants respectfully submit that the invention is distinguished over the art.

Rejections under 35 U.S.C. § 103(a)

Claims 1-7 stand rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over either Robbins *et al.*, Blood 82(4):1277-1287, 1993 or Valet in view of Chang (U.S. Pat. No. 4,591,570). Claims 1-3 and 7 stand rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Terstappen, Moreau, Matutes, or Kurec, in view of Chang.

Applicants respectfully traverse these grounds for rejection. In short the Action has alleged that the claims are obvious in the light of the above-referenced art. As indicated above, the documents cited by the Action relate to two or three immunocytometric techniques to identify a particular leukemia cell. This is not a pattern recognition assay, as presently claimed. This is in effect detecting the presence or absence of particular cells or using the antibodies to capture a cell carrying a particular CD antigen so that it may be identified by other means. Applicants are strongly of the view that the Action is engaging in improper hindsight reconstruction in raising allegations of obviousness. There is a subtle yet significant difference between detecting the presence or absence of a CD antigen and detecting a pattern of CD antigens which includes both the presence or absence of particular antigens as well as relevant numbers of certain antigens. Again, this is well highlighted in the enclosed Venn diagrams. Applicants do not consider that a person of ordinary skill in the art upon reading any of the prior art documents cited by the Action would be motivated to develop a pattern recognition assay as

instantly claimed. Accordingly, Applicants respectfully submit that this ground for rejection has been overcome and thus request withdrawal of this rejection.

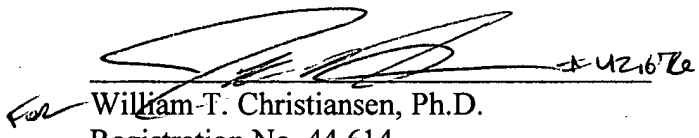
The Commissioner is authorized to charge any additional fees due by way of this Amendment, or credit any overpayment, to our Deposit Account No. 19-1090.

Applicants respectfully submit that the claims remaining in the application are now allowable. Favorable consideration and a Notice of Allowance are earnestly solicited.

Respectfully submitted,

Richard Ian Christopherson et al.

SEED Intellectual Property Law Group PLLC



For William T. Christiansen, Ph.D.
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WTC:jto

Enclosure:
Postcard
Appendix I (Exhibits, 7 Sheets)
Appendix II (Belov et al., 7 Sheets)

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